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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 10:28:22 ON 29 JAN 2004

FILE 'CAPLUS' ENTERED AT 10:28:22 ON 29 JAN 2004
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FILE 'BIOSIS' ENTERED AT 10:28:22 ON 29 JAN 2004
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FILE 'BIOTECHDS' ENTERED AT 10:28:22 ON 29 JAN 2004
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=> s DSP-15 polypeptide
L1             1 DSP-15 POLYPEPTIDE

=> d l1 ibib ab

L1    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-13578  BIOTECHDS
TITLE:            New dual-specificity phosphatase 15 polypeptide and
                  polynucleotides, useful for treating e.g. Duchenne muscular
                  dystrophy, cancer, graft-versus-host disease, autoimmune
                  diseases, allergies, metabolic diseases;
                     vector-mediated recombinant protein gene transfer and
                     expression in host cell, antisense and antibody for use in
                     drug screening and abnormal cell growth and abnormal cell
                     proliferation therapy
AUTHOR:           LUCHE R M; WEI B
PATENT ASSIGNEE:  CEPTYR INC
PATENT INFO:      WO 2002024740 28 Mar 2002
APPLICATION INFO: WO 2000-US29406 19 Sep 2000
PRIORITY INFO:    US 2001-955732 18 Sep 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2002-394127 [42]
AB    DERWENT ABSTRACT:
      NOVELTY - A new isolated dual-specificity phosphatase 15 (DSP-
      15) polypeptide (I) comprising: (a) a 659-amino acid
      sequence (P1) given in the specification, (b) a sequence of a DSP
      alternate form comprising 471 amino acids (P2); or (c) a variant of (a)
      or (b) differing in one or more amino acid deletions, additions,
      insertions or substitutions of no more than 50% of the residues in (P1)
      or (P2), where the polypeptide retains the ability to dephosphorylate an
      activated MAP-kinase.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
      following: (1) an isolated polynucleotide encoding (I) or at least 10 or
      15 consecutive amino acid residues of (I): (2) an isolated polynucleotide
      that detectably hybridizes to the complement of fully defined sequence of
      1980 (S1) or 1416 (S2) bp given in the specification, under conditions
      that include a wash in 0.1X SSC and 0.1% SDS at 50 degrees C for 15 min;
      (3) an expression vector comprising the polynucleotide; (4) a host cell
      transformed or transfected with the expression vector; (5) an antisense
      polynucleotide comprising at least 15 consecutive nucleotides
      complementary to a polynucleotide encoding (I); (6) a method of producing
      a (I); (7) an isolated antibody, or antigen binding fragment that
      specifically binds to (I); (8) a pharmaceutical composition comprising an
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antibody or its fragment in combination with a carrier; (9) a method for detecting DSP-15 expression in a sample; (10) a method for screening for an agent that modulates DSP-15 activity; (11) methods for modulating proliferative response, differentiation or survival of a cell by contacting a cell with an agent that modulates DSP-15 activity; (12) a method of treating a patient afflicted with a disorder associated with DSP-15 activity by administering a modulator of DSP-15 activity; (13) a DSP-15 or DSP-15 alternate form substrate trapping mutant polypeptide that differs from (I) by one or more amino acid deletions, additions, insertions or substitutions in no more than 50% of the residues in (P1), where the polypeptide binds to a substrate with an affinity that is not substantially diminished relative to DSP-15, and the ability of the polypeptide to dephosphorylate a substrate is reduced relative to DSP-15; and (14) a method for screening a molecule for the ability to interact with DSP-15.

BIOTECHNOLOGY - Preferred Polypeptide: The substrate trapping mutant polypeptide contains a substitution at position 382 or position 413 of P1. Preferred Polynucleotide: The polynucleotide encoding P1 and P2 comprises S1 and S2, respectively. Preparation: (I) is produced by culturing a host cell defined above for the expression of the **DSP -15 polypeptide**, and isolating **DSP-15 polypeptide** from the host cell culture. Preferred Methods: Detecting DSP-15 expression in a sample comprises contacting a sample with an antibody or an antigen-binding fragment to allow formation of an antibody/DSP-15 or antibody/DSP-15 alternate complex, detecting the level of the complex formed in the sample. The antibody is linked to a support material or to a detectable marker. The biological sample is obtained from a patient. Alternatively, the method comprises contacting the sample with an antisense polynucleotide, and detecting in the sample an amount of DSP-15 or DSP alternate form polynucleotide that hybridizes to the antisense polynucleotide, and detecting the expression of DSP-15 or its alternate form in the sample. The amount of DSP-15 polynucleotide or its alternate form that hybridizes to the antisense polynucleotide is determined by PCR or a hybridization assay. The sample comprises an RNA or cDNA preparation. Screening for an agent that modulates the activity of DSP-15 or its alternate form comprises contacting a candidate agent with (I) to permit interaction between the polypeptide and candidate agent, and evaluating the ability of the polypeptide to dephosphorylate a substrate of DSP-15 or its alternate form, relative to a predetermined ability of the polypeptide to dephosphorylate the substrate in the absence of the candidate agent. The DSP-15 or DSP-15 alternate form substrate is a MAP-kinase, and the candidate agent is a small molecule present within a combinatorial library. The method may alternatively comprise contacting a candidate agent with a cell comprising a DSP-15 or DSP-15 alternate form promoter operably linked to a polynucleotide encoding a detectable transcript or protein to allow interaction between the promoter and candidate agent, and subsequently evaluating the expression of the polynucleotide relative to a predetermined level of expression in the absence of candidate agent. The polynucleotide encodes a **DSP-15 polypeptide**, a DSP-15 alternate form, or a reporter protein. Modulating a proliferative response, differentiation of survival of a cell comprises contacting the cell with an agent that modulates of the activity of DSP-15 or its alternate form, where the agent modulates a pattern of gene expression, apoptosis, or cell cycle. The cell displays contact inhibition of cell growth, anchorage independent growth, or an altered intercellular adhesion property. The cell is preferably present within a patient. Screening a molecule for the ability to interact with DSP-15 or DSP-15 alternate form comprises contacting a candidate molecule with (I) to allow the candidate molecule and polypeptide to interact, detecting the presence or absence of binding of the candidate molecule to the polypeptide by affinity purification step, yeast two hybrid screening or screening of a phage display library, and determining if the candidate molecule interacts with DSP-15 or DSP-15 alternate form.

ACTIVITY - Cytostatic; Immunosuppressive; Antiallergic. No

supporting data provided.

MECHANISM OF ACTION - DSP-15 modulator. No supporting data provided.

USE - DSP-15 polypeptides may be used to identify agents that modulate DSP-15 activity, where such agents may inhibit or enhance signal transduction via a MAP-kinase cascade, leading to cell proliferation. DSP polypeptides, modulating agents, and/or polynucleotides encoding the polypeptides may be used to modulate DSP-15 activity in a patient, and to ameliorate disorders such as Duchenne muscular dystrophy, cancer, graft-versus-host disease, autoimmune diseases, allergies, metabolic diseases, abnormal cell growth, abnormal cell proliferation and cell cycle abnormalities. DSP-15 alternate form polypeptides are useful in screening assays for modulators of enzyme activity and/or substrate binding (all claimed).

ADMINISTRATION - Administration can be topical, oral, nasal, intrathecal, rectal, vaginal, sublingual, or parenteral (e.g. subcutaneous, intravenous, intramuscular, intrasternal, intracavernous, intrameatal, or intraurethral injection or infusion). Dosage is 0.01-100 mug per kg body weight, preferably 0.1-10 mug.

EXAMPLE - To derive a longer consensus DSP amino acid sequence motif that would be useful for the identification of new dual-specificity phosphatase (DSP) family members, multiple known human DSP sequences were aligned and compared. An alignment of 8 amino acid sequences derived from 8 human DSPs having MAP-kinase phosphatase activity yielded a conserved homology region consisting of a 24-amino acid peptide sequence containing the PTP active site signature motif. A candidate peptide having the sequence NGRVLVHCQAGISRSGTNILAYLM was used to search the Expressed Sequence Tag database. Search results identified EST AK001790, which was aligned with several known PTPs including VHR and several DSPs and included a PTP active site motif within a larger domain that was not conserved when compared to the other DSP active site domains. The active amino acid sequence of the DSP-like active site domain encoded AK001790, VLVHCKMGVSRSAATVLAYAMK, was resubmitted to a BLAST search of the GenBank EST database and identified 2 ESTs having sequence overlaps with AK001790: AW952870 and AW326161. when AW952870 was submitted to BLAST search, its first 355 nucleotides were found to contain exon sequences encoded in the human HTGS entry AP001885. Querying the GenBank EST database with AW326151 as a BLAST search identified AW732634 as an additional related human EST, which contained a 284 nucleotide overlap with AW326161. AW732634 also exhibited a 60 nucleotide overlap with AW952870 and contained exon sequences encoded in the HTGS entry AP001885. The derived sequence from AW952870 and AW732634 was used to design a 5' RACE primer. 5' and 3' RACE analysis was performed using brain, testis, and skeletal muscle cDNA templates with 5'/3' RACE kits. PCR and RACE reactions were performed using the PCR-5' primer and GSP2.5 primer, and the reaction products were sequenced. A cDNA (consisting of 1980 bp) encoding a protein of 659 amino acids was identified as DSP-15, and a second cDNA (consisting of 1416 bp) encoding a protein of 471 amino acids was also identified as a DSP-15 alternate form, apparently a truncated form produced by alternate splicing of DSP-15 encoding transcript. (91 pages)

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=> s Dual specificity polypeptide
L2            0 DUAL SPECIFICITY POLYPEPTIDE

=> s Dual specificity phosphatase?
L3         1211 DUAL SPECIFICITY PHOSPHATASE?

=> dup rem l3
PROCESSING IS APPROXIMATELY  97% COMPLETE FOR L3
PROCESSING COMPLETED FOR L3
L4           430 DUP REM L3 (781 DUPLICATES REMOVED)

=> s l4 and dna
L5           153 L4 AND DNA
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=> s l5 and dual specificity phosphatase-15
L6            1 L5 AND DUAL SPECIFICITY PHOSPHATASE-15

=> d his

     (FILE 'HOME' ENTERED AT 10:27:51 ON 29 JAN 2004)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, BIOTECHDS' ENTERED AT 10:28:22 ON
     29 JAN 2004
L1             1 S DSP-15 POLYPEPTIDE
L2             0 S DUAL SPECIFICITY POLYPEPTIDE
L3          1211 S DUAL SPECIFICITY PHOSPHATASE?
L4           430 DUP REM L3 (781 DUPLICATES REMOVED)
L5           153 S L4 AND DNA
L6             1 S L5 AND DUAL SPECIFICITY PHOSPHATASE-15

=> focus l5
PROCESSING COMPLETED FOR L5
L7           153 FOCUS L5 1-

=> d l7 1-10 ibib ab

L7   ANSWER 1 OF 153  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:585464  CAPLUS
DOCUMENT NUMBER:          138:180209
TITLE:                    Separation of Cdc25 dual specificity
                          phosphatase inhibition and DNA
                          cleaving activities in a focused library of analogs of
                          the antitumor antibiotic Dnacin
AUTHOR(S):                Wipf, Peter; Hopkins, Corey R.; Phillips, Eleanor O.;
                          Lazo, John S.
CORPORATE SOURCE:         Department of Chemistry, University of Pittsburgh,
                          Pittsburgh, PA, 15260, USA
SOURCE:                   Tetrahedron (2002), 58(32), 6367-6372
                          CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER:                Elsevier Science Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Biol. evaluation of 96 analogs and synthetic intermediates of the
     naphthyridinomycin-type antitumor antibiotic Dnacin led to the
     identification of several low-micromolar inhibitors of dual
     specificity phosphatases, specifically Cdc25A1, Cdc25B2,
     and VHR, as well as the tyrosine phosphatase PTP1B.  While the parent
     Dnacins are potent DNA cleavage agents, most of the analog
     structures, even those that retained significant phosphatase inhibitory
     activities, did not lead to plasmid DNA cleavage.  Thus, the
     DNA-targeting and the phosphatase-inhibitory activities of Dnacins
     can be assigned to different pharmacophores.
REFERENCE COUNT:          59    THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 2 OF 153  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2001:731028  CAPLUS
DOCUMENT NUMBER:          135:284076
TITLE:                    Protein and cDNA sequences of novel human dual
                          specificity phosphatase sequence
                          homologs and uses thereof
INVENTOR(S):              Meyers, Rachel A.
PATENT ASSIGNEE(S):       Millennium Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 143 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   20
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073059	A2	20011004	WO 2001-US9477	20010323
WO 2001073059	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002065406	A1	20020530	US 2001-815419	20010322
EP 1319078	A2	20030618	EP 2001-922645	20010323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-191858P P 20000324
WO 2001-US9477 W 20010323

AB The invention provides protein and cDNA sequences of human proteins, designated 38692 or 21117, which have sequence homol. with **dual specificity phosphatase** family members. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. 38692 or 21117 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 38692 or 21117 gene has been introduced or disrupted. The invention still further provides isolated 38692 or 21117 proteins, fusion proteins, antigenic peptides and anti-38692 or 21117 antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

L7 ANSWER 3 OF 153 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:646042 CAPLUS
DOCUMENT NUMBER: 133:236826
TITLE: DSP-1 **dual-specificity phosphatase**
INVENTOR(S): Luche, Ralf M.; Wei, Bo
PATENT ASSIGNEE(S): Ceptyr, Inc., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053636	A2	20000914	WO 2000-US6154	20000308
WO 2000053636	A3	20010215		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-123255P P 19990308

AB Compns. and methods are provided for the treatment of conditions assocd. with cell proliferation, cell differentiation and/or cell survival. In particular, the **dual-specificity phosphatase** DSP-1, and polypeptide variants thereof that stimulate dephosphorylation of DSP-1 substrates, are provided. The polypeptides may be used, for

example, to identify antibodies and other agents that inhibit DSP-1 activity. The polypeptides and agents may be used to modulate cell proliferation, cell differentiation and cell survival for such disorders include cancer, graft-vs-host disease, autoimmune disease, allergies, metabolic disease, and abnormal cell growth or proliferation, and cell cycle abnormalities..

L7 ANSWER 4 OF 153 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:731029 CAPLUS
DOCUMENT NUMBER: 135:284077
TITLE: Protein and cDNA sequences of a novel human **dual specificity phosphatase** sequence homologs and uses thereof
INVENTOR(S): Meyers, Rachel A.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073060	A2	20011004	WO 2001-US9603	20010322
WO 2001073060	A3	20020404		
WO 2001073060	C2	20021219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002065406	A1	20020530	US 2001-815419	20010322
EP 1268818	A2	20030102	EP 2001-920760	20010322

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-191858P P 20000324
WO 2001-US9603 W 20010322

AB The invention provides protein and cDNA sequences of a novel human protein, designated 18221, which has sequence homol. with **dual specificity phosphatase** family members. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. 18221 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 18221 gene has been introduced or disrupted. The invention still further provides isolated 18221 proteins, fusion proteins, antigenic peptides and anti-18221 antibodies. Diagnostic methods utilizing compns. of the invention are also provided. The invention also provides methods of modulating the differentiation and proliferation of hematopoietic cells (e.g., erythroid cells) utilizing the compns. of the invention. Accordingly, methods of treating, preventing and/or diagnosing hematopoietic disorders are disclosed.

L7 ANSWER 5 OF 153 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927611 CAPLUS
DOCUMENT NUMBER: 138:19529
TITLE: Antisense modulation of dual specific phosphatase 5 expression for treatment of hyperproliferative disorders
INVENTOR(S): Monia, Brett P.; Watt, Andrew T.
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097108	A2	20021205	WO 2002-US15305	20020515

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003060437	A1	20030327	US 2001-865993	20010525

PRIORITY APPLN. INFO.: US 2001-865993 A 20010525

AB Antisense compds., compns. and methods are provided for modulating the expression of dual specific phosphatase 5. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding dual specific phosphatase 5. Methods of using these compds. for modulation of dual specific phosphatase 5 expression and for treatment of diseases assocd. with expression of dual specific phosphatase 5 are provided.

L7 ANSWER 6 OF 153 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:625037 CAPLUS
DOCUMENT NUMBER: 138:20113
TITLE: Analysis of gene associated with exogenous nucleic acid improving repair of intestinal epithelium after .gamma. irradiation in mice
AUTHOR(S): Cui, Daxiang; Zeng, Guiying; Wang, Feng; Tian, Furong; Guo, Yanhai; Xu, Junrong; Yan, Xiaojun; Ren, Dongqing; Su, Chengzhi
CORPORATE SOURCE: Institute of Genetic Diagnosis, Fourth Military Medical University, Xi'an, 710033, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Jinzhan (2001), 28(3), 353-357
CODEN: SHYCD4; ISSN: 1000-3282
PUBLISHER: Shengwu Huaxue Yu Shengwu Wuli Jinzhan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The mol. mechanism of exogenous nucleic acids improving repair of irradn.-damaged intestinal epithelium was studied. 45 Mice being irradiated by .gamma. ray were treated with 40 .mu.g small intestinal RNA as test group, whose small intestinal specimens were collected resp. at 6 h, 12 h, 24 h, 4 d and 8 d after treatment; 40 mice being irradiated by .gamma. ray were treated with physiol. saline as control group, whose small intestinal specimens were collected at the same interval time. Then fragments of genes expressed in test group higher than those in control group, were obtained by using LD-PCR based on subtractive hybridization. After that, these gene fragments were cloned into T vectors, and were sequenced. Obtained sequences were searched for GenBank. 90 Clones assocd. with repair of irradn.-damaged crypt cells were obtained. In test group of 6 h, higher similar sequences mainly were as follows: mRNA for heat shock protein, Nmi mRNA, Dutt1 protein, mRNA for Na, K-ATPase gamma subunit, mRNA for heat shock protein, finger type transcript factor, porcine growth hormone-releasing hormone gene, Homo sapiens **dual specificity phosphatase**, etc. In test group of 12 h, higher similar sequences were as follows: alk. phosphatase mRNA, alk.

phosphatase 2, glkA gene, single stranded replicative centromeric gene, Homo sapiens DMBT1 candidate tumor gene, tRNA-Met gene, mouse Ig unrearranged transcribed H-chain, thyroxine-binding globulin gene, alpha-2- plasmin inhibitor gene. In test group of 24 h, higher similar sequences were as follows: anti-CEA ScFv antibody heavy chain vary region, anti-**DNA** antibody Ig heavy chain, mRNA for Ig kappa chain region, anti- BONT/A Hc ScFv antibody heavy chain vary region, mRNA for ScFv collagenase heavy chain vary region, AE0199 Ig heavy chain, mouse Ig gamma-chain, Ig rearranged gamma-chain mRNA, anti- NP antibody IgH, mRNA for arginine/serine kinase, **dual specificity phosphatase**, family mRNA telomerase-assocd. protein, anti-human erB-2 region, BMP-4 gene. In test group of 4 d, higher similar sequences were as follows: mRNA for sodium channel, tazarotene-induced gene, betaine- GABA transporter gene, homobox protein Xgbx-2 mRNA, mRNA for stress-activated protein, FK506 binding protein, calcium/calmodulin dependent gene, PEST phosphatase interactin gene, haptoglobin mRNA. In test group of 8 d, higher similar sequences were as follows: Ig Mu variable region mRNA, Mus musculus Ig K chain mRNA- V-region, mRNA for Hox1b protein, Mus musculus neutroactin mRNA, rat alk. phosphatase mRNA, Human mRNA for XP-C repair complementing protein, human alpha-2-plasmin inhibitor gene, mRNA for CCAT binding factor, mouse active H-chain VJ region, etc. Eighteen were new sequences, whose function were unclear. Ninety clones were obtained to be assocd. with repair of damaged mice intestinal gland cells caused by .gamma. ray and treated by small intestinal RNA. Repair of damaged intestinal gland cells treated by exogenous nucleic acids may be assocd. with hsp, Nmi, Dutt1, alk. phosphatase genes and eighteen new sequences.

L7 ANSWER 7 OF 153 MEDLINE on STN

ACCESSION NUMBER: 97184169 MEDLINE
DOCUMENT NUMBER: 97184169 PubMed ID: 9030581
TITLE: Molecular cloning and functional characterization of a novel mitogen-activated protein kinase phosphatase, MKP-4.
AUTHOR: Muda M; Boschert U; Smith A; Antonsson B; Gillieron C; Chabert C; Camps M; Martinou I; Ashworth A; Arkinstall S
CORPORATE SOURCE: Geneva Biomedical Research Institute, Glaxo Wellcome Research and Development S.A., CH-1228 Plan-les-Ouates, Geneva, Switzerland.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Feb 21) 272 (8) 5141-51.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y08302
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970403

AB Extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK), and p38/RK/CSBP (p38) mitogen-activated protein (MAP) kinases are target enzymes activated by a wide range of cell-surface stimuli. Recently, a distinct class of **dual specificity phosphatase** has been shown to reverse activation of MAP kinases by dephosphorylating critical tyrosine and threonine residues. By searching the expressed sequence tag data base (dbEST) for homologues of known **dual specificity phosphatases**, we identified a novel partial human sequence for which we isolated a full-length cDNA (termed MKP-4). The deduced amino acid sequence of MKP-4 is most similar to MKP-X/PYST2 (61% identity) and MKP-3/PYST1 (57% identity), includes two N-terminal CH2 domains homologous to the cell cycle regulator Cdc25 phosphatase, and contains the extended active site sequence motif VXVHCXAGXSRSXTX3AYLM (where X is any amino acid) conserved in **dual specificity**

phosphatases. MKP-4 produced in Escherichia coli catalyzes vanadate-sensitive breakdown of p-nitrophenyl phosphate as well as in vitro inactivation of purified ERK2. When expressed in COS-7 cells, MKP-4 blocks activation of MAP kinases with the selectivity ERK > p38 = JNK/SAPK. This cellular specificity is similar to MKP-3/PYST1, although distinct from hVH-5/M3-6 (JNK/SAPK = p38 >>> ERK). Northern analysis reveals a highly restricted tissue distribution with a single MKP-4 mRNA species of approximately 2.5 kilobases detected only in placenta, kidney, and embryonic liver. Immunocytochemical analysis showed MKP-4 to be present within cytosol although punctate nuclear staining co-localizing with promyelocytic protein was also observed in a subpopulation (10-20%) of cells. Chromosomal localization by analysis of DNAs from human/rodent somatic cell hybrids and a panel of radiation hybrids assign the human gene for MKP-4 to Xq28. The identification and characterization of MKP-4 highlights the emergence of an expanding family of structurally homologous **dual specificity phosphatases** possessing distinct MAP kinase specificity and subcellular localization as well as diverse patterns of tissue expression.

L7 ANSWER 8 OF 153 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2001-02628 BIOTECHDS
TITLE: **Dual specificity phosphatase**-8 (DSP-8) which dephosphorylates mitogen-activated protein-kinase, used to identify agents that inhibit DSP-8 activity and modulate cell proliferation, differentiation, and survival;
vector-mediated gene transfer, expression in host cell, antibody, antisense oligonucleotide, **DNA** probe and **DNA** primer for drug screening and disease gene therapy
AUTHOR: Luche R M; Wei B
PATENT ASSIGNEE: Ceptyr
LOCATION: Bothel, WA, USA.
PATENT INFO: WO 2000063393 26 Oct 2000
APPLICATION INFO: WO 2000-US10508 19 Apr 2000
PRIORITY INFO: US 1999-130173 20 Apr 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-687181 [67]
AB An isolated **dual specificity phosphatase**-8 (DSP-8) (I) which a defined sequence of 190 amino acids (S2)(specified, or its variants, that differs in 1 or more amino acid deletions, additions or substitutions at no more that 50% of the residues in (S2)), such that the protein retains the ability to dephosphorylate a mitogen-activated protein (MAP) kinase (EC-2.7.1.37) is claimed. Also claimed are: a **DNA** (II) that encodes at least 10-15 consecutive amino acids of a protein having a sequence corresponding to (S2); a vector (III) containing (II); a host cell transformed with (III); a **DNA** (IV) that encodes (I); a vector (V) that has (IV); a host cell (VI) transformed with (V); an antisense **DNA** containing 15 consecutive nucleotides complementary to (VI); a **DNA** that detectably hybridizes to the complement of (IV); an antibody that binds to (I); a pharmaceutical composition containing the antibody; and screening an agent that modulates activity of (I). DSP-8 modulating agents are useful for treating Duchenne muscular dystrophy, cancer, allergies, metabolic disease, abnormal cell growth and cell cycle abnormalities. The antisense DNAs can be used as **DNA** probe or **DNA** primers. (65pp)

L7 ANSWER 9 OF 153 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-19558 BIOTECHDS
TITLE: Novel isolated **dual specificity phosphatase** polypeptide, 18221 useful for treating 18221-mediated or related disorders such as hematopoietic disorders or erythroid-associated disorders;

vector-mediated gene transfer, expression in host cell and antibody for recombinant protein production, drug screening and disease therapy

AUTHOR: MEYERS R A
PATENT ASSIGNEE: MEYERS R A
PATENT INFO: US 2002065406 30 May 2002
APPLICATION INFO: US 2000-815419 24 Mar 2000
PRIORITY INFO: US 2001-815419 22 Mar 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-565749 [60]

AB DERWENT ABSTRACT:

NOVELTY - Isolated **dual specificity phosphatase** polypeptide (I), termed 18221 having a sequence (S1) of 217 amino acids encoded by a nucleic acid molecule (NA) that hybridizes to a NA having a sequence (S2) of 1292 or 654 base pairs or its complement, or a polypeptide encoded by a NA 80% identical to S2, or fragment of S1, where S1, S2 are given in specification, is new.

DETAILED DESCRIPTION - An isolated **dual specificity phosphatase** polypeptide (I), termed 18221 comprises an allelic variant of a polypeptide having a sequence (S1) of 217 amino acids encoded by a nucleic acid molecule (NA) that hybridizes to a NA having a sequence (S2) of 1292 or 654 base pairs or its complement, or a polypeptide encoded by a NA 80% identical to S2, or fragment of S1, where S1, S2 are given in specification, is new. (I) is selected from a naturally occurring allelic variant of S1 encoded by a NA which hybridizes to NA comprising S2 (or its complement) under stringent conditions, a polypeptide encoded by a NA comprising a sequence which is at least 80% identical to S2, and a fragment comprising at least 15 contiguous amino acids of S1. INDEPENDENT CLAIMS are included for the following: (1) an isolated NA (II) selected from a NA comprising a sequence at least 80% identical to S2, a NA comprising a fragment of at least 462 nucleotides of S2, a NA which encodes a polypeptide comprising S1, or its fragment comprising 15 contiguous amino acids of S1, and a NA which encodes a naturally occurring allelic variant of a polypeptide comprising S2, where the NA hybridizes to a NA comprising S2 (or its complement), under stringent conditions; (2) a host cell (III) containing (II); (3) an antibody (IV) which selectively binds (I); (4) production of (I); (5) detecting (M1) the presence of (II) in a sample by contacting the sample with a nucleic acid probe or primer which selectively hybridizes to (II), and determining whether the probe or primer binds to (II) in the sample; (6) a kit (V) comprising a compound which selectively binds to (I) or hybridizes to (II), and instructions for use; (7) modulating (M2) the activity of (I) by contacting (I) or a cell expressing (I) with a compound which binds to (I); (8) modulating (M3) hematopoiesis by contacting a hematopoietic cell with an agent that modulates the activity or expression of (I) or (II), thus modulating the proliferation, differentiation or survival of the hematopoietic cell; and (9) treating (M4) or preventing a hematopoietic disorder in a subject, by administering to the subject a compound that modulates the activity or expression of (I).

WIDER DISCLOSURE - Also disclosed are: (1) a nucleic acid construct that includes (II); (2) a vector containing (II); (3) an isolated NA antisense to (II); (4) an assay for determining the presence or absence of a genetic alteration in (I) or (II); (5) a NA that differs from S2 due to degeneracy of the genetic code; (6) detectably labeled oligonucleotide primer and probe molecules; (7) 18221 chimeric or fusion proteins; (8) a fragment of (IV); (9) a NA which encodes (IV); (10) a vector which includes the above NA; (11) a cell transformed with the above NA; (12) a cell line, e.g., hybridoma, for producing (V); (13) a non-human transgenic animal in which a 18221 gene has been introduced or disrupted; (14) a population of cells from the above transgenic animal; (15) an agent which modulates expression or activity of (I) or (II); (16) a computer medium having a number of digitally encoded data records; (17) a two dimensional array having a number of addresses; (18) a method of

evaluating a sample or subject; (19) a method of analyzing 18221; (20) a method of making computer readable record of a 18221 sequence; (21) a machine-readable medium for holding instructions for performing a method for determining whether a subject has a 18221-associated disease or disorder or a pre-disposition to the disease or disorder; and (22) a method for determining whether a subject has a 18221-associated disease or disorder or a pre-disposition to the disease or disorder, provided in an electronic system and/or in a network.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (III) under conditions in which (II) is expressed. Preferred Polypeptide: (I) further comprises heterologous amino acid sequences. Preferred Polynucleotide: (II) further comprises vector nucleic acid sequences and a sequence encoding a heterologous polypeptide. Preferred Cell: (III) is a mammalian host cell, preferably a non-human mammalian host cell.

ACTIVITY - Cytostatic; Immunosuppressive; Antidiabetic; Antirheumatic; Antiarthritic; Antiulcer; Antiasthmatic; Antianemic; Antiallergic; Neuroprotective; Antiinflammatory. No supporting data provided.

MECHANISM OF ACTION - Modulator of the activity of (I); modulator of hematopoiesis (claimed); gene therapy; modulator of growth factor activity; modulator of intracellular pathway; modulator of cell differentiation; stimulator of hematopoiesis; modulator of cell proliferation; modulator of cell apoptosis; inactivator cell surface growth factor receptors. No supporting data provided.

USE - The anti-18221 antibody (IV) is useful for detecting the presence of (I) in a sample by contacting the sample with (IV), and determining whether (IV) binds to (I) in the sample. (I) is useful for identifying a compound which binds to (I) or modulates the activity of (I). (I), or its encoding polynucleotide (II) are useful for evaluating the efficacy of a treatment of a hematopoietic disorder, and for diagnosing or staging a hematopoietic disorder in a subject (all claimed). (I) or (II) is useful for treating 18221-mediated or related disorders, e.g., hematopoietic disorders including neoplastic hematopoietic or immune disorders (e.g., erythroid leukemia, myelodysplastic syndrome) and non-neoplastic hematopoietic disorders or diseases (autoimmune diseases such as diabetes mellitus, rheumatoid arthritis, multiple sclerosis, Crohn's disease, ulcerative colitis, asthma, aplastic anemia, allergy) or erythroid-associated disorders such as hemolytic anemia or erythrocytosis. (I), (II) or (IV) is useful in screening assays, detection assays (e.g., chromosomal mapping, tissue typing, forensic biology), predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenomics), and in methods of treatment (e.g., therapeutic and prophylactic). (I) or (IV) is useful as reagents or targets in assays applicable to treatment and diagnosis of 18221-mediated or related disorders. (I) or (II) is useful as query sequences to perform a search against public databases to, for e.g., identify other family members or related sequences. (I) is useful as an immunogen to generate antibodies that bind (I). (I) is useful to screen for naturally occurring 18221 substrates, and to screen for drugs or compounds which modulate 18221 activity. (I) is useful as a bait protein in a yeast two-hybrid or three-hybrid assay and to identify other proteins which bind to or interact with 18221 and or involved in the 18221 activity. (II) is useful as hybridization probe to identify (II), or as polymerase chain reaction (PCR) primer for the amplification or mutation of (II). (II) is useful in gene therapy, to express (I), to detect 18221 mRNA or a genetic alteration in a 18221 gene, and to modulate 18221 activity. (II) is useful to map their respective genes on a chromosome, e.g. to locate gene regions associated with genetic disease or to associate 18221 with the disease, to identify an individual from a minute biological sample (tissue typing), and to aid in forensic identification of the biological sample. (IV) is useful to isolate and purify (I), to detect (I) and to diagnostically monitor protein levels in tissue as part of a clinical testing procedure.

ADMINISTRATION - A pharmaceutical composition comprising (I), its encoding polynucleotide (II) or an anti-18221 antibody (IV) is

administered by parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, or rectal route at a dose of 0.001-30 mg/kg, preferably 1-10 mg/kg, more preferably 5-6 mg/kg for (I) and (II) and 10 to 20mg/kg for (IV).
EXAMPLE - No relevant example is given. (61 pages)

L7 ANSWER 10 OF 153 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:401491 BIOSIS
DOCUMENT NUMBER: PREV200300401491
TITLE: Characterization and potential regulation of **dual specificity phosphatases** MKP-3 by platelet-derived growth factor in mesangial cells.
AUTHOR(S): Popovic, Aleksandra [Reprint Author]; Pesic, Miodrag; Pratt, Phillip F.
CORPORATE SOURCE: Pharmacology and Toxicology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI, 53226, USA apopovic@mcw.edu; mpesic@mcw.edu; ppratt@mcw.edu
SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 648.11. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Sep 2003
Last Updated on STN: 3 Sep 2003

AB **Dual-specificity phosphatases** negatively regulate mitogen activated protein kinases like ERK1/2, p38 and JNK and may serve as key anti-proliferative enzymes to balance proliferation with apoptosis and quiescence. Platelet-derived growth factor (PDGF) has been implicated as a key agent in proliferative disorders such as restenosis and glomerulonephritis. This project tested the hypothesis that PDGF regulates the expression and/or activity of MKP-3, a specific phosphatase for ERK. Primary mesangial cell (MC) cultures were used in combination with Western blot, RT-PCR and proliferation assays. Western blot analysis detected MKP-3 in rat MC lysates. MKP-3 mRNA, assessed by RT-PCR, was upregulated by 30 minutes after treatment with 10% fetal bovine serum but was only marginally increased after 1 h treatment with PDGF (25 ng/mL). PDGF stimulated a profound increase in the phosphorylation of ERK that decreased over time but remained above control for at least 6 h. Co-immunoprecipitation studies detected association of MKP-3 with ERK at all time points examined. Rat MC were successfully infected with an adenovirus encoding a myc-tagged MKP-3. Experiments are planned to determine the effects of adenoviral-delivered MKP-3 on PDGF-stimulated proliferation and phosphorylation of ERK. This work begins to address potentially important function(s) of **dual specificity phosphatases** in the regulation of growth factor signaling.

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(FILE 'HOME' ENTERED AT 10:27:51 ON 29 JAN 2004)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, BIOTECHDS' ENTERED AT 10:28:22 ON 29 JAN 2004

L1 1 S DSP-15 POLYPEPTIDE
L2 0 S DUAL SPECIFICITY POLYPEPTIDE
L3 1211 S DUAL SPECIFICITY PHOSPHATASE?
L4 430 DUP REM L3 (781 DUPLICATES REMOVED)
L5 153 S L4 AND DNA
L6 1 S L5 AND DUAL SPECIFICITY PHOSPHATASE-15
L7 153 FOCUS L5 1-

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